

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph at page 2, lines 7-8, as follows.

We have now discovered that introduction of a halogen atom at a particular ring position produces an ~~order of magnitude~~ increase in potency against cathepsin K.

Please delete the table, at page 54, line 9, to page 64, line 2, and insert the following therefor.

No.	Structure	P2	P3 building block	MS data
8.1		A	Ac ₂ O	301 [M+H] ⁺
8.2		A		353 [M+H] ⁺
8.3		A		353 [M+H] ⁺
8.4		A		363 [M+H] ⁺

No.	Structure	P2	P3 building block	MS data
8.5		A		383 [M+H] ⁺
8.6		A		402 [M+H] ⁺
8.7		A		405 [M+H] ⁺
8.8		A		416 [M+H] ⁺
8.9		A		419 [M+H] ⁺
8.10		A		420 [M+H] ⁺

No.	Structure	P2	P3 building block	MS data
8.11		A		433 [M+H] ⁺
8.12		A		435 [M+H] ⁺ 453 [M+18] ⁺
8.13		A		464 [M+H] ⁺
8.14		B	-	393 [M+H] ⁺
8.15		A		542 [M+H] ⁺ 560 [M+18] ⁺

No.	Structure	P2	P3 building block	MS data
8.16		A		544 [M+H] ⁺ 562 [M+18] ⁺
8.17		A		566 [M+H] ⁺ 584 [M+18] ⁺
8.18		A		598 [M+H] ⁺ 616 [M+18] ⁺
8.19		A		545 [M+H] ⁺ 563 [M+18] ⁺
8.20		C		556 [M+H] ⁺ 574 [M+18] ⁺
8.21		A		588 [M+H] ⁺ 606 [M+18] ⁺

No.	Structure	P2	P3 building block	MS data
8.22		A		489 [M+18-morpholine] ⁺ 471 [M+H-morpholine] ⁺
8.23		A		472 [M+H] ⁺ 490 [M+18] ⁺
8.24		A		446 [M+H] ⁺ 464 [M+18] ⁺
8.25		A		560 [M+18] ⁺ 473 [M+H-morpholine] ⁺

No.	Structure	P2	P3 building block	MS data
8.32		A		$[M+H]^+$ 471 $[M+18]^+$ 489
8.33		A		$[M+H]^+$ 483 $[M+18]^+$ 501
8.34		A		$[M+H]^+$ 517 $[M+18]^+$ 535
8.35		A		$[M-H]^-$ 529 $[M+18]^+$ 549
8.36		A		$[M+H]^+$ 532 $[M+18]^+$ 550
8.37		A		$[M+H]^+$ 546 $[M+18]^+$ 564

No.	Structure	P2	P3 building block	MS data
8.38		A		$[M+H]^+$ 504 $[M+18]^+$ 521
8.39		A		$[M+H]^+$ 445 $[M+18]^+$ 463
8.40		A		$[M+H]^+$ 503 $[M+18]^+$ 521
8.41		A		$[M+H]^+$ 533 $[M+18]^+$ 551
8.42		A		$[M+H]^+$ 547 $[M+18]^+$ 565
8.43		A		$[M+H]^+$ 532 $[M+18]^+$ 550

No.	Structure	P2	P3 building block	MS data
8.44		A		489 [M+18-morpholine] ⁺ 471 [M+H-morpholine] ⁺
8.45		A		560 [M+18] ⁺ 473 [M+H-morpholine] ⁺
8.46		A		[M+H] ⁺ 533 [M+18] ⁺ 551
8.47		A		[M+H] ⁺ 531 [M+18] ⁺ 549

No.	Structure	P2	P3 building block	MS data
8.48		A		$[\text{M}+\text{H}]^+$ 529 $[\text{M}+18]^+$ 547
8.49		A		$[\text{M}+\text{H}]^+$ 489 $[\text{M}+18]^+$ 507
8.50		A		$[\text{M}+\text{H}]^+$ 531 $[\text{M}+18]^+$ 549
8.51		A		$[\text{M}+\text{H}]^+$ 475 $[\text{M}+18]^+$ 493
8.52		A		$[\text{M}+\text{H}]^+$ 565 $[\text{M}+18]^+$ 583

No.	Structure	P2	P3 building block	MS data
8.53		A		$[M+H]^+$ 503 $[M+18]^+$ 521
8.54		A		$[M+H]^+$ 544 $[M+18]^+$ 562
8.55		A		$[M+H]^+$ 503 $[M+18]^+$ 521
8.57		A		$[M+H]^+$ 543 $[M+18]^+$ 561
8.59		A		$[M+H]^+$ 538 $[M+18]^+$ 556

No.	Structure	P2	P3 building block	MS data
8.60		A		$[M+H]^+$ 529 $[M+18]^+$ 547
8.61		A		$[M+H]^+$ 501 $[M+18]^+$ 519
8.62		A		$[M+H]^+$ 515 $[M+18]^+$ 533
8.64		A		$[M+H]^+$ 538 $[M+18]^+$ 556
8.65		A		$[M+H]^+$ 525 $[M+18]^+$ 543

Please amend the paragraph at page 65, lines 5-15, as follows.

Solid phase synthesis of ~~8.1-8.13 & 8.15-8.67~~ 8.1-8.13, 8.15-8.55, 8.57, 8.59-8.62, 8.64 & 8.65 was generally carried out using Murphy's linker methodology using known chemistries as described in WO02/88106. The ketone function of the FmocNH bicyclic was derivatised as an acid labile semicarbazone which provided a carboxylic acid for attachment to the aminomethyl functionalised polymer support resin using HBTU, HOBr and NMM. After Fmoc removal the corresponding P2 Fmoc acid was coupled on where the symmetric anhydride was preformed. Coupling was first carried out for 8 h, and then repeated with fresh reagents overnight. After Fmoc removal the P3 acids were introduced using standard coupling conditions. Washing, drying and cleavage from the resin provided the crude desired material which was purified either by column chromatography or preparative hplc. Compounds which required modified procedures are described below.

Please amend the paragraph at page 94, lines 25-26, as follows.

Yields of the following title compounds in examples ~~8.53-8.61 and 8.63~~ 8.53-8.55, 8.57 and 8.59-8.61 were in general between 30 and 90%.

Please amend the paragraph at page 95, lines 20-27, as follows.

4-(2-Piperidin-4-yl-thiazol-4-yl)-benzoic acid (Example 8.56)

4-Thiocarbamoyl-piperidine-1-carboxylic acid tert-butyl ester (2.47 mmol) and 4-(2-Bromo-acetyl)-benzoic acid (2.47 mmol) were mixed in THF (12 mL). After stirring at room temperature for 5 minutes the mixture was heated to 80 °C for 2 hours. The volume was reduced to 5 mL and diethylether (5 mL) was added. The mixture was then cooled to -20 °C and filtered. The solid was washed with a small amount of diethylether and dried. m/z = 289.1 in MS ES+, which was characterized by hplc and MS and used in the next step without any further purification.

Please amend the paragraph at page 96, lines 4-10, as follows.

4-[2-(Pyridin-3-ylamino)-thiazol-4-yl]-benzoic acid (Example 8.58)

Pyridin-3-yl-thiourea (2.06 mmol) and 4-(2-Bromo-acetyl)-benzoic acid (2.06 mmol) were mixed in THF (12 mL). After stirring at room temperature for 5 minutes the mixture was heated

to 80 $^{\circ}$ C for 2 hours. The mixture was then cooled to room temperature and filtered. The solid was washed with a small amount of diethylether and dried. m/z = 298.0 in MS ES+, which was characterized by hplc and MS and used in the next step without any further purification.

Please amend the paragraph at page 97, lines 19-33, as follows.

4-[2-(1-Methyl-pyrrolidin-3-yl)-thiazol-5-yl]-benzoic acid (Example 8.63)

3-Thiocarbamoyl-pyrrolidine-1-carboxylic acid tert-butyl ester (2.47 mmol) 4-(2-Bromo-acetyl)-benzoic acid (2.47 mmol) were mixed in THF (12 mL). After stirring at room temperature for 5 minutes the mixture was heated to 80 $^{\circ}$ C for 1 hour. The mixture was then cooled to room temperature and filtered. The solid was washed with a small amount of diethylether and dried. m/z = 304.1 in MS ES+. This solid was then mixed in dichloromethane-trifluoroacetic acid (2:1) and kept at room temperature for 20 minutes. The mixture was concentrated to near dryness and the concentrated once from dichloromethane and once from 1 N HCl in diethylether. The remaining solid was mixed with acetic acid (0.5 mL), methanol (3 mL) and tetrahydrofuran (4.5 mL) and formaldehyde (aq. 37%, 300 mL) and polystyrene bound cyanoborohydride (2.36 mmol/g, 900 mg) was added. The slurry was then agitated for 16 hours at room temperature. The slurry was then filtered and the resin washed with methanol (2 mL). The solution was concentrated to dryness *in vacuo*. m/z = 289.0 in MS ES+, which was characterized by hplc and MS and used in the next step without any further purification.

Please amend the paragraph at page 103, lines 2-3, as follows.

It will be apparent that introduction of at least one halogen atom to P1, according to the invention has surprisingly resulted in ~~a 10 fold an~~ increase in potency.